

**WHAT IS CLAIMED IS:**

1. A unit dose which is comprised of activated protein C, at least one prodrug, or at least one functional variant thereof, wherein the activated protein C, the prodrug, or the functional variant is present in an effective amount to provide neuroprotection in a subject who needs treatment.
2. The unit dose of Claim 1 which results in at least reduced or insignificant systemic anticoagulation when administered to the subject.
3. The unit dose of Claim 1, wherein the subject has a neurodegenerative disease.
4. The unit dose of Claim 3, wherein the neurodegenerative disease is selected from the group consisting of Alzheimer's disease, Down syndrome, Huntington's disease, and Parkinson's disease.
5. The unit dose of any one of Claims 1-4, wherein the effective amount is from 0.02 milligrams to 0.04 milligrams of the activated protein C per kilogram of body weight of the subject, or an equivalent amount of the prodrug or the functional variant.
6. The unit dose of any one of Claims 1-4, wherein the effective amount is at most 0.02 milligrams of the activated protein C per kilogram of body weight of the subject, or an equivalent amount of the prodrug or the functional variant.
7. The unit dose of any one of Claims 5-6, wherein the unit dose is administered to the subject in less than 72 hours.
8. A pharmaceutical composition which is comprised of activated protein C, at least one prodrug, or at least one functional variant thereof wherein the activated protein C, the prodrug, or the functional variant is present in an

effective amount to provide neuroprotection for stressed or injured cells in a subject.

9. The composition of Claim 8, wherein the composition is adapted for delivery to the subject's brain.

10. The composition of any one of Claims 8-9, wherein the effective amount is from 0.02 milligrams to 0.04 milligrams of the activated protein C per kilogram of body weight of the subject, or an equivalent amount of the prodrug or the functional variant thereof.

11. The composition of any one of Claims 8-9, wherein the effective amount is at most 0.02 milligrams of the activated protein C per kilogram of body weight of the subject, or an equivalent amount of the prodrug or the functional variant thereof.

12. A method of providing treating cell stress or injury which is comprised of administering an effective amount of activated protein C, at least one prodrug, or at least one variant thereof to a subject such that at least one effect of stress or injury is improved in one or more cell types of the subject.

13. The method of Claim 12, wherein the activated protein C, the prodrug, or at least one variant thereof is derived from human protein C or variant thereof, and the subject is a human.

14. The method of any one of Claims 12-13, wherein the one or more cell types are in the subject's brain.

15. The method of any one of Claims 12-14, wherein the subject is in need of treatment because of brain radiation injury.

16. The method of any one of Claims 12-14, wherein the cellular stress or injury is caused by at least one selected from the group consisting of reduced

hemoperfusion, hypoxia, ischemia, ischemic stroke, radiation, oxidants, reperfusion injury, and trauma.

17. The method of any one of Claims 12-16, wherein the effective amount is from 0.02 milligrams to 0.04 milligrams of the activated protein C per kilogram of body weight of the subject, or an equivalent amount of the prodrug or the functional variant.

18. The method of any one of Claims 12-16, wherein the effective amount is at most 0.02 milligrams of the activated protein C per kilogram of body weight of the subject, or an equivalent amount of the prodrug or the functional variant.

19. The method of any one of Claims 12-18, wherein the effective amount of the activated protein C, the prodrug, or the functional variant does not provide a therapeutic effect in the subject as an anticoagulant, profibrinolytic, or antithrombotic agent.

20. The method of any one of Claims 12-18, wherein the at least one function variant is comprised of at least one mutation selected from the group consisting of activated protein C (APC) mutants KKK191-193AAA and RR229/230AA.

21. Use of activated protein C, at least one prodrug, or at least one functional variant thereof in an amount effective to reduce p53 signaling in at least one cell type of a subject.

22. The use of Claim 21, wherein NF- $\kappa$ B signaling is not significantly affected.

23. Use of activated protein C, at least one prodrug, or at least one functional variant thereof for the manufacture of a pharmaceutical composition to inhibit p53 signaling activity in apoptotic cells.

24. A process of screening for an agent which provides neuroprotection comprising:
- (a) providing a library of candidate agents which are variants of activated protein C and/or protein C,
  - (b) determining p53 signaling activity in one or more stressed or injured cells in the presence of a candidate agent,
  - (c) selecting at least one agent by its ability to inhibit p53 signaling activity in the one or more stressed or injured cells, and
  - (d) confirming that the selected agent at least inhibits cell death or promotes cell survival.
25. A process of screening for an agent which provides neuroprotection comprising:
- (a) providing a library of candidate agents which are variants of activated protein C and/or protein C,
  - (b) determining activity of one or more receptors selected from the group consisting of protease activated receptor-1 (PAR-1), protease activated receptor-3 (PAR-3), and endothelial protein C receptor (EPCR) in one or more stressed or injured brain cells in the presence of a candidate agent,
  - (c) selecting at least one agent because it is an agonist of PAR-1 and/or PAR-3 and/or EPCR in the one or more stressed or injured brain cells, and
  - (d) confirming that the selected agent at least inhibits brain cell death and/or promotes brain cell survival.
26. An agent produced by the process of any one of Claims 24-25.
27. Use of an agonist of protease activated receptor-1 (PAR-1) and/or protease activated receptor-3 (PAR-3) and/or endothelial protein C receptor (EPCR) in an effective amount to provide neuroprotection in a subject in need of treatment.
28. The use of Claim 27, wherein the agonist is a TFLLRNPNDK peptide.